The IP Management of the PRSV-Resistant Papayas Developed by Cornell University and the University of Hawaii and Commercialized in Hawaii

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ABSTRACT

In the late 1990s, a consortium of public sector organizations commercialized the first and still-major food biotechnology product developed by public sector organizations. The author represented the Papaya Administrative Committee, an organization of papaya growers in Hawaii, in obtaining patent licenses necessary for the commercial introduction of a disease-resistant transgenic papaya. This chapter describes the approach taken in deciding what patents needed to be licensed, how the licenses were obtained, and how they were administered.

1. INTRODUCTION

In the fall of 1995, I was retained by papaya growers in Hawaii to provide legal assistance on patent and licensing issues related to a transgenic, disease-resistant papaya that had been developed for use in Hawaii. Although this technology was developed by Dennis Gonsalves while at Cornell University along with researchers in Hawaii, my client was actually the Papaya Administrative Committee (PAC) in Hilo, Hawaii. PAC had been created many years earlier under a federal marketing order by the U.S. Department of Agriculture (USDA) to assist the Hawaiian papaya industry in marketing papaya.

As a result of the devastating effect of papaya ringspot virus (PRSV) on the industry, PAC undertook to obtain the patent licenses necessary for commercial introduction of the transgenic, disease-resistant papaya. As PAC's legal advisor, I was required to identify which patent rights needed to be licensed, to negotiate and obtain licenses, and to help PAC administer the licenses that were obtained. This paper describes how I assisted PAC with these tasks and brings to light some practical considerations relating to the patenting and licensing of transgenic plant technology.

2. IDENTIFICATION OF PATENT RIGHTS THAT NEEDED TO BE LICENSED

Under 35 U.S.C. § 271, a U.S. patent gives its owner the right to prevent others from making, using, selling, or offering to sell the subject matter of the patent in the United States. The recipient of a license of such patent rights has the ability to engage in at least some of these activities without risking an injunction and/or being held liable for damages. PAC wanted to be able to go forward quickly with the transgenic papaya without fear of such risks. Therefore, my first task was to determine which patent rights needed to be licensed by PAC.

The task involved determining which patents would be infringed by the transgenic papaya technology in the absence of a license. In order to proceed, it was first necessary to identify which technology was used in making the transgenic papaya. Based on the findings, a group of patents was identified that potentially needed to

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be licensed. Such identification of candidate patents often requires conducting an infringement search on computer databases and in the U.S. Patent and Trademark Office (PTO). In the case of transgenic papaya, we also had some guidance from industry sources. Once a group of candidate patents was identified, I proceeded with the legal analysis to determine which of those patents would actually be infringed.

The exclusionary rights afforded by a U.S. patent are defined by the claims. Therefore, in analyzing a patent for infringement, it is first necessary to interpret the scope of the patent (in other words, the claims of the patent). This involves examining the literal language of the claims, reviewing the specification (or the body) of the patent, and studying the prosecution history of the corresponding patent application (in other words, the correspondence to and from the PTO during the patent application process). Through this analysis, the meaning of the terms in the patent claims and, accordingly, the scope of the claims as a whole is determined. With this information, it can then be decided whether the claims are infringed by the subject technology. A U.S. patent can be directly infringed in two ways:

- by literal infringement
- under the doctrine of equivalents

Literal infringement occurs if the language of the claims covers, literally, the subject technology. The absence of literal infringement does not, however, mean that infringement is avoided. Infringement can occur under the doctrine of equivalents if the differences between the subject technology and the claimed invention are insubstantial. One approach to determining whether infringement has occurred under the doctrine of equivalents is to analyze whether the subject technology and the patented invention do substantially the same thing in substantially the same way to achieve substantially the same results. The scope of the doctrine of equivalents is limited by what the prior art teaches and by what the patentee surrendered during prosecution of the patent.

In the context of a patent covering a transgenic plant, infringement can occur if a party makes, uses, or sells that plant. These actions constitute direct infringement (see Figure 1). Even if there have been no acts of direct infringement by a particular party, liability can ensue if that party induces or contributes to another's acts of direct infringement.

"Inducing infringement" occurs when one party aids and abets the direct infringing acts of another. Such liability can occur in the context of patents covering a method of making transgenic plants disease resistant (Figure 2). Researchers who are making such transgenic plants using a particular vector would be directly infringing such a patent. However, the supplier of this vector would not be directly infringing but could be liable for inducing infringement if the vector is provided with instructions to use it in order to produce disease-resistant transgenic plants.

"Contributory infringement" occurs when a party sells a nonstaple article of commerce which has no substantial noninfringing use. In the context of a patent covering a method of making a transgenic plant that is disease resistant, a party planting seeds for such transgenic plants would be a direct infringer. However, a party selling seeds for such plants, though not liable for direct infringement, would have contributory infringement liability (Figure 3).

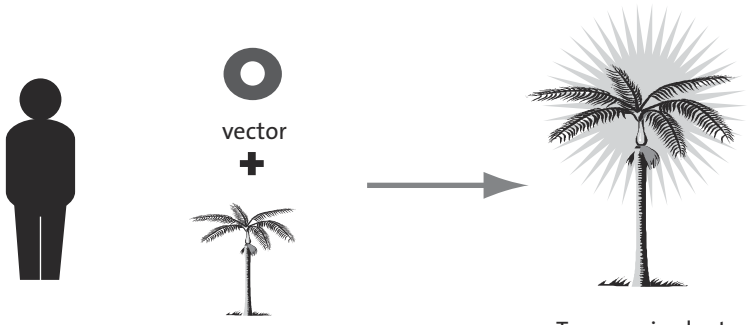
The technology used by Dennis Gonsalves and colleagues to develop a transgenic papaya, in brief, consisted of the preparation of a vector and the introduction of it into papaya by biolistic transformation.[1] The vector, a map of which is shown in Figure 4 was an *Agrobacterium*-binary vector which included the 35S promoter, the 5' untranslated leader sequence, the PRSV coat protein encoding gene, and the β-glucoronidase (GUS) gene. Thus, we needed to consider licensing patent rights relating to various DNA components, plant transformation procedures, modes of plant disease-resistance mediation, and transgenic plants.

With the assistance of Dennis Gonsalves, I analyzed the technology utilized in developing the transgenic, disease-resistant papaya and determined which of the candidate patents needed to be licensed. It was determined that licenses were needed from Company Y for patent rights

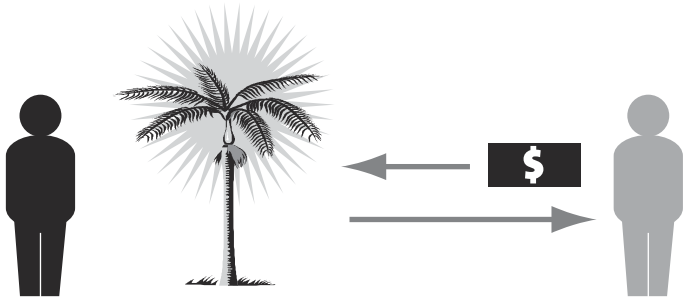
Figure 1: Acts of Patent Infringement in the United States Include Direct Infringement

Direct Infringement
U.S. Patent No. 1
Claim: Transgenic Plant

MAKING



SELLING



USING

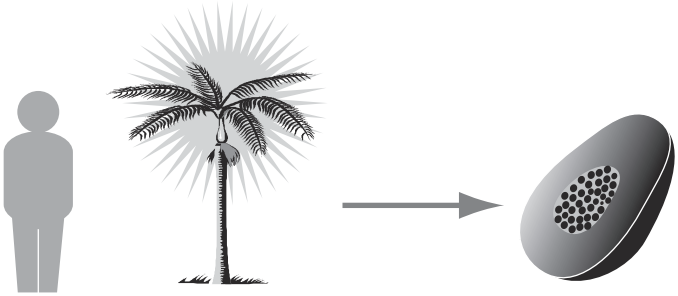


Figure 2: Acts of Contributory Patent Infringement in the United States

Contributory Infringement

U.S. Patent No. 1
Claims:
1. Process of Producing a Disease Resistant Plant Comprising
    a. Providing a Transgenic Plant and
    b. Planting the Transgenic Plant whereby the Plant is Disease Resistant

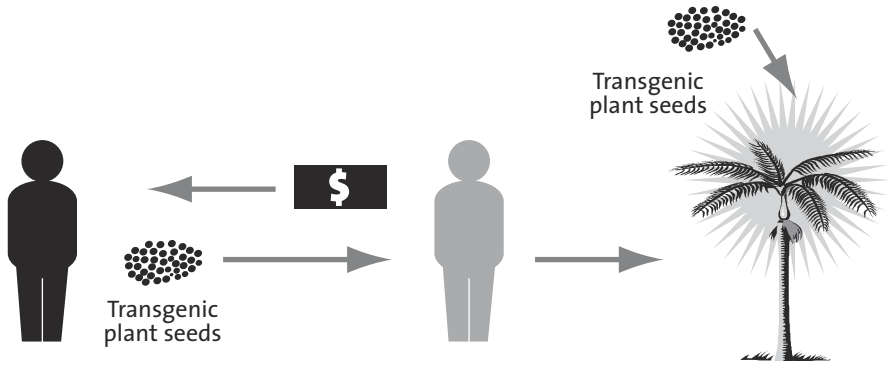


Figure 3: Acts of Inducement to Infringe in the United States

Inducement to Infringe

U.S. Patent No. 1
Claims:
1. Process of Producing a Disease Resistant Plant Comprising
    a. Providing a Transgenic Plant and
    b. Planting the Transgenic Plant whereby the Plant is Disease Resistant

Product Literature
Uses of Vector:
- Incorporating Plant Trait Gene in Plant
- Incorporating Virus Gene in Plant

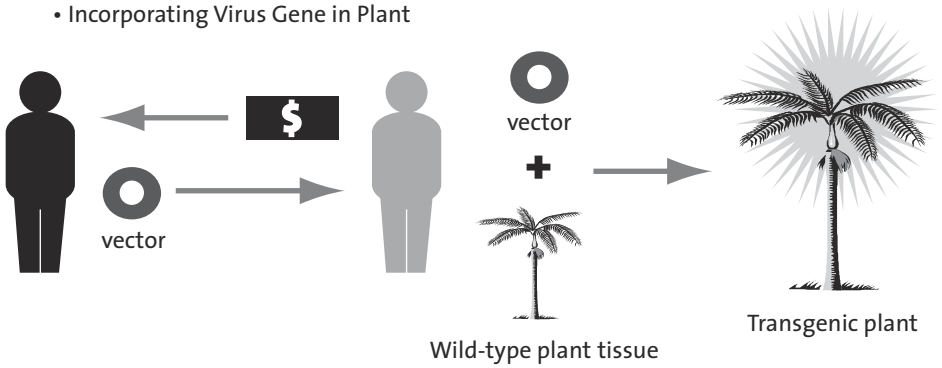
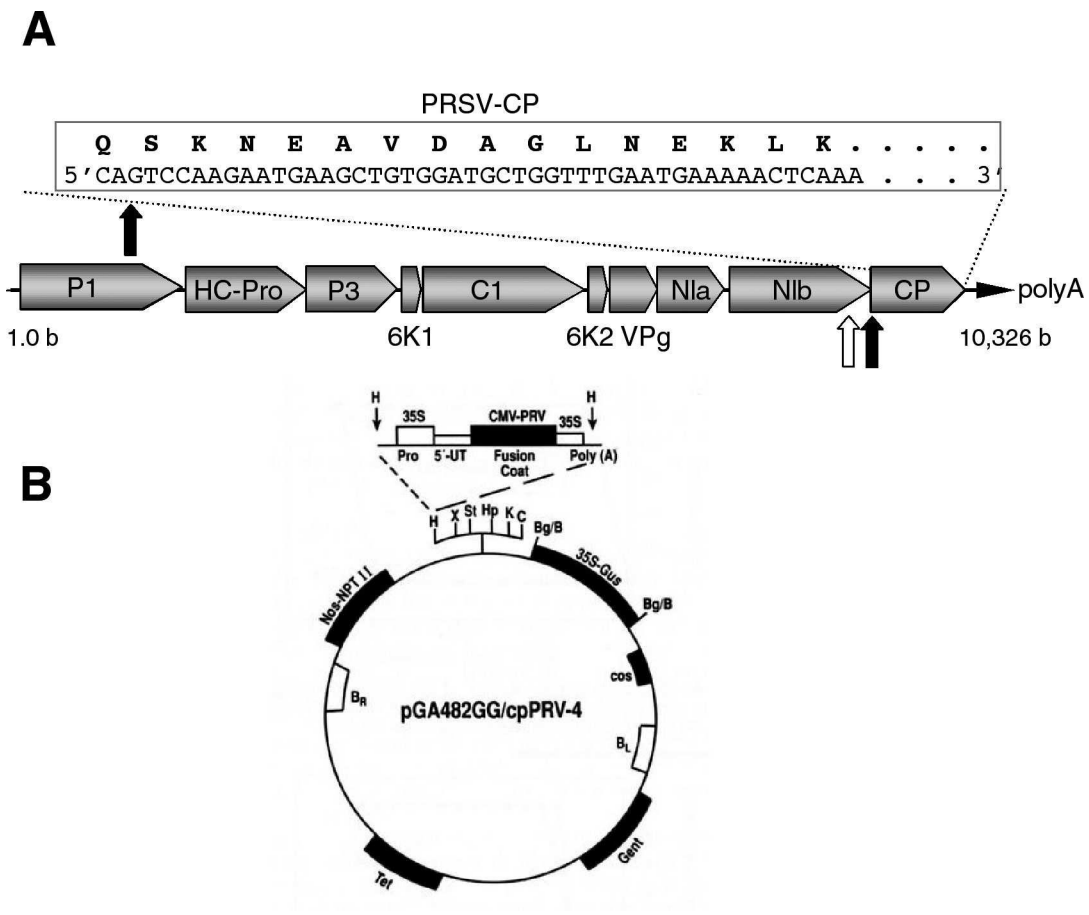


Figure 4: Agrobacterium Binary Vector pGA482GG/cpPRV-4



Organization and proteolytic protein products of the 10, 326 base monocistonic PRSV genome. (A) Shown in detail, the N-terminal sequence of the coat, the protein (PRSV-CP). Box arrows represent the proteolytic sites producing the mature coat protein (CP).(B) Map of the functional genes of the Agrobacterium transformation vector pGA482GG/cpPRV-4 used for PRSV-resistant papaya. The coat protein gene cassette consists of the coat protein structural gene of PRSV HA 5-1 translationally fused to the N-terminal end of the cucumber mosaic virus coat protein (CMV-CP), including the translation initiation codon, the CMV 5' untranslated sequence (5' UTR), and the Cauliflower Mosaic Virus 35S promoter. The PRSV-CP gene cassette is flanked by selectable and visible marker genes, neo (encoding NPTII) and gus, respectively. BR and BL are the left and right borders of the transformation vector T-DNA sequence.

Source: Courtesy Dennis Gonsalves (November 2006).

relating to various components of the vector and the general mode of plant disease resistance. From Massachusetts Institute of Technology (M.I.T.), PAC decided to license rights to the 5' untranslated leader sequence. Company X had rights to technology to impart resistance to PRSV by use of a gene from the virus. We wanted to license that technology. We also wanted rights to the GUS gene from Cambia Biosystems LLC (Canberra, Australia). For various reasons, we decided that licenses were not needed for other candidate patents.

3. LICENSE NEGOTIATIONS

After identifying which patent rights PAC should license, the next job was to obtain the necessary licenses. This proved to be a very difficult task because the parties had different strategic objectives.

PAC wanted to be able to distribute transgenic papaya seed without charging recipients and without having to maintain the accounting records normally needed for licenses involving a royalty on net sales. Therefore, we sought licenses involving a one-time, up-front payment. With this approach, PAC also wanted to be assured that it would receive licenses under any patents infringed by the transgenic papaya that issued after the license agreement was signed. Otherwise, PAC would be at risk of having to negotiate a new license and making further payments to a party that had already granted a license to PAC. Another issue was PAC's financial resources. Since PAC's licensing activities were financed by public funds and contributions from its members, many of whom were farmers in Hawaii, the licensing fees needed to be manageable. While PAC needed a substantial level of accommodation from licensors on financial issues, its demands on the scope of any grant under a license agreement were modest. In particular, PAC needed to obtain the right to grow transgenic papaya plants in Hawaii and to sell the resulting fruit worldwide. Finally, since PAC did not itself grow or sell papaya, it needed to be able to sublicense its rights to constituents, including growers.

All of the licensors were sympathetic to the need to introduce a transgenic, disease-resistant papaya in Hawaii. However, each had its own strategic interests, which needed to be protected. Some licensors did not, at that time, have a policy of or experience with licensing out, and they were reluctant to proceed with setting a corporate-wide strategy based on a license for a very small crop. Undoubtedly, there was concern over having any deal with PAC dictate which terms would have to be offered for future licenses on strategically important crops. Many of the individuals working on business development for the licensors were very busy and did not have much time to focus efforts on a deal for a very small crop with potentially little economic return. Some licensors had a tremendous commitment to developing a plant biotechnology business and wanted to ensure that any licensees of its rights did not jeopardize the industry as a whole. Lastly, the licensors needed to know that the financial terms of any license were fair. Given the relatively low strategic interest a transgenic papaya license had to the licensors, PAC had to engage in an extensive effort to educate them about the Hawaiian papaya industry, the impact of PRSV in Hawaii, and the benefit of the transgenic papaya to papaya growers in Hawaii. In particular, we tried to gain sympathy from the licensors by explaining that the virus had devastated the Hawaiian papaya industry and that the transgenic papaya needed to be introduced in Hawaii to ensure that farmers could maintain their livelihood. Our promotional efforts often led to questions about PAC's purpose and membership. When the licensors saw that large, well-known fruit packing companies were members of PAC, there were usually questions from the licensors about who was being aided by the licenses. However, we were able to explain that the true beneficiaries of the licenses were growers whose farms were being severely hurt by PRSV.

In some cases, sympathy for the plight of growers was not sufficient and the licensors needed to be further motivated. The USDA was helpful in several instances. Because it is an important regulatory agency in the plant biotechnology industry, the licensors wanted to remain in the USDA's good graces in order to avoid jeopardizing regulatory approvals for their own projects. Since the USDA created PAC, was already

actively involved in the Hawaiian papaya industry, and wanted to see the transgenic, disease-resistant papaya introduced in Hawaii, the agency was very willing to help PAC. Without that help, a number of the licenses may never have been obtained.

Once we had communicated with the licensors, we were generally able to persuade them to prepare a draft license agreement from which license negotiations could proceed. Although we usually prefer to generate the first draft of a license agreement, doing so tends to be more costly, and we were trying to limit PAC's costs for the project. In any event, once the initial draft license agreement was received, we proceeded with license negotiations and ultimately were able to enter into license agreements with all of the targeted licensees.

Company X was anxious to put the transgenic papaya on the market as a philanthropic effort and was PAC's first licensor.

Cambia Biosystems LLC is a technology licensing company without any particular interest in exploiting the GUS gene technology in the plant biotechnology industry. They were interested in helping the Hawaiian papaya industry, as long Cambia could be assured of a fair deal, from an economic standpoint. Cambia was our next licensee.

Company Y was sympathetic to the plight of the Hawaiian papaya industry, but as a result of the company's extensive involvement in the transgenic plant industry, its strategic interests were the most difficult to harmonize. Once the company was able to resolve its objectives, it moved enthusiastically forward with license negotiations. It regarded the license to be negotiated with PAC as a prototype for future deals involving outlicensing of Company Y technology. Company Y became PAC's third licensor.

The last license was obtained from M.I.T., which had no particular strategic concerns about licensing in the plant biotechnology industry but was concerned about whether a paid-up license provided fair compensation. We ultimately were able to develop an arrangement by which M.I.T. could be assured of an economically fair deal.

As a result, PAC had obtained the licenses it needed to begin growing transgenic papaya in Hawaii. Shortly after the last license agreement was executed, PAC began distribution of transgenic papaya seed to growers. The commercial use of this product of biotechnology has had a substantial beneficial economic impact on the Hawaiian papaya industry.

4. LESSONS LEARNED

There are a number of lessons to be learned from the transgenic-papaya licensing effort. These lessons, relating to both patent and licensing issues, can benefit researchers, technology transfer professionals, business people, and lawyers. Researchers in the transgenic biotechnology area should recognize that there are patents covering many commonly used genetic components and plant transformation procedures. The manufacture, use, sale of, or offer to sell such patented materials by researchers without a research license is an act of direct patent infringement. Engaging in any of these activities would put the researchers' employers at risk of being sued and having to pay the patentees' damages, as well as attorneys' fees. If the researcher were employed at an academic institution, the prospect of incurring such expenses would be daunting. Even if a research license were obtained, it would not allow introduction of the product of research into a commercial product. Any effort to do so would be an act of patent infringement. In the case of an academic institution working with commercial entities, the licensing out of technology utilizing the patent rights of others, or the transfer of materials incorporating patented subject matter, also raises issues of patent infringement. In particular, the institution can be deemed to be inducing infringement (aiding and abetting the infringing acts of another) or engaging in contributory infringement (selling or offering to sell a material having no substantial use other than in conjunction with a patented process). To avoid these issues, researchers should use unpatented or easily licensed technology wherever possible.

On the other hand, developers of technology wishing to enhance their licensing royalties

and their leverage over competitors may wish to make their technology freely available once the necessary patent applications have been filed. The widespread use of such technology can lead to its adoption as an industry standard for which substantial licensing revenue can be derived. Moreover, the use of a company's patented technology in the commercial product of a competitor can give the company significant leverage over the competitor in accessing technology owned by the competitor, in maximizing royalty payments from the competitor, and in preventing the competitor from introducing an important commercial product.

In licensing patent rights from others, it is important to examine what the various patents you are considering would actually cover. In the transgenic plant industry, there is a great deal of "street talk" about patents and what they purport to cover. Reliance on "scuttlebutt" could result in the procurement of and payment for licenses on patent rights that are not needed. On the other hand, failure to obtain all the necessary licenses raises the threat of an injunction, of liability for damages, and of the costs of litigation. A careful analysis of the patent landscape is well worth the expense. Entities licensing technology on behalf of others need to properly control how it makes the technology available. In the case of PAC, it has made transgenic papaya seed available to growers only after they attend an educational program and sign a material transfer/sublicense agreement with PAC. Likewise, researchers wishing to obtain transgenic papaya seed from PAC are required to sign a material transfer/research sublicense agreement with PAC. These measures were undertaken to ensure that growers and researchers understood the obligations pursuant to the license agreements and complied with those obligations.

5. CONCLUSION

The above events may not be of great economic significance to global agriculture. However, as one of the first efforts to develop a transgenic fruit crop, procure the necessary licenses, and introduce a product into commerce, Hawaii's transgenic papaya story is certainly an important event for the plant biotechnology industry. The successful results achieved by PAC may well serve as a model for future transgenic plant technology. ■

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1 See Ling K, S Namba, C Gonsalves, JL Slightom and D Gonsalves. 1991. Protection Against Detrimental Effects of Potyvirus Infection in Transgenic Tobacco Plants Expressing the Papaya Ringspot Virus Coat Protein Gene. *Bio/Technology* 9:752–758. See also Fitch M, RM Manshardt, D Gonsalves, JL Slightom and JC Sanford. 1992. Virus Resistant Papaya Plants Derived from Tissues Bombarded with the Coat Protein Gene of Papaya Ringspot Virus. *Bio/Technology* 10:1466–1472.